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Drug Induced Sleep Endoscopy in the decision-making process of children with obstructive sleep apnea

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Highlights

1. Sleep endoscopy (SE) allows the planning of surgical treatment of pediatric Obstructive Sleep Apnea (OSA).

2. OSA persists after tonsillectomy and adenoidectomy (T&A) in about third of cases.
3. The two-thirds of naive cases presents hypertrophic tonsils and/or adenoids at SE.
4. SE may be of benefit when clinical evaluation is unremarkable or in cases of OSA after T&A.

Abstract

Tonsillectomy and adenoidectomy (T&A) is currently recommended in children with Obstructive Sleep Apnea (OSA). However, the condition persists after surgery in about one third of cases. It has been suggested that Drug Induced Sleep Endoscopy (DISE) may be of help for planning a more targeted and effective surgical treatment but evidence is yet weak. The aim of this review is to draw recommendation on the use of DISE in children with OSA. More specifically, we aimed at determine the proportion of cases whose treatment may be influenced by DISE findings. A comprehensive search of articles published from February 1983 to January 2014 listed in the PubMed/MEDLINE databases was performed. The search terms used were: "endoscopy" or "nasoendoscopy" or "DISE" and "obstructive sleep apnea" and "children" or "child" or "pediatric". The main outcome was the rate of naive children with hypertrophic tonsils and/or adenoids. The assumptions are that clinical diagnosis of hypertrophic tonsils and/or adenoids is reliable and does not require DISE and that exclusive T&A may solve OSA in the vast majority of cases even in the presence of other concomitant sites of obstruction. Five studies were ultimately selected and all were case series. The median (range) number of studied children was 39 (15-82). Mean age varied from 3.2 to 7.8 years. The combined estimate rate of OSA consequent to hypertrophic tonsils and/or adenoids was 71% (95%CI: 64-77%). In children with Down Syndrome, the combined estimated rate of hypertrophic tonsils and/or adenoids was 62% (95%CI: 44-79%).

Our findings show that DISE may be of benefit in a minority of children with OSA since up to two thirds of naive cases presents with hypertrophic tonsils and/or adenoids. Its use should be limited to those whose clinical evaluation is unremarkable or when OSA persists after T&A.

Key words: endoscopy / nasoendoscopy / DISE / obstructive sleep apnea / children

1. Introduction

Sleep-disordered breathing (SDB) is a common entity in children and comprehends the continuum of sleep-related breathing disturbances including Obstructive Sleep Apnea (OSA) [1]. It has been estimated that OSA affects approximately 1.2% to 5.7% of all children [2,3] and it is now widely recognized as a cause of significant morbidity [4,5]. Untreated OSA can result in serious complications such as neurocognitive and behavioural disturbances [6,7], failure to thrive [8], enuresis [9] and cardiovascular dysfunction including systemic and pulmonary hypertension [10], ventricular remodelling [11] and endothelial dysfunction [12]. The most accurate and comprehensive method for the diagnosis and evaluation of severity of OSA is full-night polysomnography (PSG) [3].

Hypertrophy of adenotonsillar tissue is an undisputed major contributor to the development of OSA

in otherwise healthy children. Accordingly, the practice guidelines established by the American Academy of Pediatricians recommend tonsillectomy and adenoidectomy (T&A) as the first line of treatment for childhood OSA [3,13]. Nevertheless, a recent meta-analysis of 1079 subjects found that up to 33.7% of children does not experience resolution after this surgery, thus questioning the common attitude to systematically perform T&A in affected children [14]. Noteworthy, the complexity of OSA is more clearly emerging and it is now recognized that hypertrophy of adenotonsillar tissue is not the unique cause of the condition. The anatomical sites of obstruction may be multiple and several systemic factors including obesity and specific comorbidities such as Down Syndrome, cerebral palsy and craniofacial abnormalities may contribute.

In order to decide a targeted and effective treatment plan, there is growing consensus that an in-depth upper-airway evaluation is required to properly characterize the pattern of obstruction. To this aim, Drug Induced Sleep Endoscopy (DISE), also known as sleep nasoendoscopy or sleep endoscopy, has been advocated for studying the dynamic airway in a sleep-like stage of children with OSA. Briefly, a flexible endoscope is inserted through the nose of the sedated children and is positioned on different levels of the upper airway (nasopharynx, soft palate, tonsils, tongue base, larynx and trachea) to detect mechanisms and sites of snoring and apneas. The examination requires general anestesia that is usually induced with the use of anesthetic gas agents (Nitrous oxide/O2 admixture at 30/70%) and, when an adequate level of sedation is obtained, it is maintained with an intravenous infusion of propofol (100mcg/Kg/min) and remi-fentanyl (100ng/Kg/die) [16,17]. Some authors prefer an infusion of dexmedetomidine (1-2mcg/Kg/hr) without a loading dose with a concurrent ketamine bolus of 1 mg/Kg that seems to induce less muscular relaxation and a more sustained respiratory effort [18]. The technique was first described in the late eighties [19,20] and subsequently validated in several independent studies [21-24]. However, to date, only few articles have been published in children [15-17,25-27].

Considering the potential growing role of DISE in the diagnostic armamentarium of children with OSA, we deem of relevance revising the available literature on this topic. DISE is a complex and

expensive technique requiring general anaesthesia and there is thus the need for robust evidence prior to foresee a systematic use of this instrument in the diagnostic algorithm of children with OSA. The main objective of this review is to discuss evidence on the pre-operative use of DISE in naive cases in order to clarify whether this assessment should be mandatory in all cases or, conversely, whether is has to be limited to specific subgroups of children.

2. Methods

A search of electronic database (PubMed and MEDLINE) was performed to identify the articles concerning Drug Induced Sleep Endoscopy in children using a combination of the following key words: "endoscopy" or "nasoendoscopy" or "DISE" and "obstructive sleep apnea" and "children" or "child" or "pediatric". We exclusively included articles written in the English language and published between February 1983 and January 2014. Potentially relevant articles were systematically reviewed and the relative references lists were analysed to identify additional valuable studies. Two authors (W.G and F.G.) independently assessed the eligibility of the selected studies and discrepancies between the reviewers were resolved by discussion. A binomial distribution model was used to estimate the 95% Confidence Interval (95%CI) of proportions. The main outcome considered was the rate of naive children with hypertrophic tonsils and/or adenoids. Children were included in this group regardless of the presence of other concomitant obstruction sites.

3. Results

Figure 1 illustrates the flow diagram of studies selection. Five studies were ultimately included

[15,16,19,25,26] of whom three were published during the last two years. The main characteristics of these studies are summarized in Table 1. None of them was randomized. Only data from case series is available. Three studies exclusively reported on non-operated children (naive) [15,19,26] whereas the remaining two reported on a combination of naive and previously operated children [16,25]. Data extracted from these latter two studies exclusively refer to non-operated children. The proportion of studied children with Down Syndrome is high but very heterogeneous, varying between a small minority of cases [15] to 50% [26]. The median (range) number of studied children was 39 (15-82). Mean age varied between 3.2 to 7.8 years.

Data on the frequency of OSA consequent to hypertrophic tonsils and/or adenoids is illustrated in Figure 2. The combined estimated rate was 71% (95%CI: 64-77%). Data on subgroups of children with significant comorbidities is scanty. The most significant group is represented by those with Down Syndrome (Table 1). Data on this subgroup could be retrieved from three studies [19,25,26]. The combined estimated rate of hypertrophic tonsils and/or adenoids was 62% (95%CI: 44-79%) (Figure 3).

4. Discussion

This review documented that a consistent proportion of children with OSA would not benefit from T&A. The condition is explained by obstruction not related to hypertrophic tonsils or adenoids in about one third of cases. Interestingly, our finding is in line with the above mentioned rate of persistence of OSA following T&A in children of 33.7% [14]. Our results strengthen the conclusions of this meta-analysis and strongly suggest that systematic T&A because of OSA is not justified. On the other hand, we do no believe that our data supports the systematic use of DISE in children with OSA. Clinical and endoscopic detection of hypertrophic tonsils or adenoids is a simple, reliable and economic diagnosis not requiring DISE. Moreover, advocating the systematic

use of DISE in affected children is in our view not justified because there is no evidence of benefits of the concomitant correction of other sites of obstructions that could be identified with DISE. In other words, the functionality of the apparatus following T&A may change and it cannot be excluded that OSA may be effectively cured with T&A also in the presence of other sites of obstruction. Noteworthy, it has also to be pointed out that the effectiveness of other interventions for the resolution of OSA such as lingual tonsillectomy, supraglottoplasty and cranio-facial surgery is yet to be definitely demonstrated in children [28-30]. Of further relevance here is that these interventions are more invasive and inevitably more risky.

Our analysis failed to document particular subgroups of naive children with comorbidities who may benefit from DISE. This conclusion is however not robust given that we were able to provide data only on one comorbidity (Down Syndrome) and, even for this condition, the number of analysed cases was small. The inference that can be drawn from our data is that children with Down Syndrome who have OSA is not a group requiring particular additional investigations. The frequency of hypertrophic tonsils and/or adenoids was 62% (95%CI: 44-79%), thus not markedly different to what observed in the whole cohort of studied children (71%, 95%CI: 64-77%). However, further evidence is required to definite conclusions.

Some limitations of our analysis should be recognized. Firstly, the number of selected studies was modest and the sample sizes were in most cases low. Secondly, the proportion of children with hypertrophic tonsils and/or adenoids varied significantly among the available studies, suggesting heterogeneity in the populations studied. Overall, there is the need for further evidence to draw a more precise and reliable estimate of the proportion of children with OSA who are diagnosed with tonsillar or adenoid obstruction at DISE.

In conclusion, DISE is a highly valuable instrument for an in-depth evaluation of OSA. However, further evidence from larger and properly designed studies is warranted prior to foresee a systematic use of this DISE in the decision-making process of naive children with OSA. At present, its use should be restricted to naive children without hypertrophic tonsils and/or adenoids and to those with

persistent OSA after T&A. In line with this conclusion, we also recommend that parents of children with OSA and hypertrophic tonsils and/or adenoids should be clearly informed before T&A that the obstruction may persist after the intervention.

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Figure legend

Figure 1: Flow diagram of studies selection.

Figure 2: Proportion of children with OSA who were diagnosed with tonsillar or adenoid obstruction at DISE. 95%CIs were calculated based on a binomial distribution model. Frequency varies significantly among the included studies ($p<0.001$).

Figure 3: Proportion of children with Down Syndrome and OSA who were diagnosed with tonsillar or adenoid obstruction at DISE. 95%CI was calculated based on a binomial distribution model. Frequency did not vary significantly among the included studies ($p=0.11$).

Table 1. Main characteristic of the selected studies.

Author	Country	Study design	Duration period	Age (years)	n° cases OSA	PSG (AHI)	C
Croft et al. [19], 1990	UK	prospective	n.r.	3.2	15 naive	n.r.	
Myatt et al. [25], 2000	Australia	prospective	n.r.	6.3	7 naive 2 post AT 2 pharyngoplasty (9 OAA)	AHI>30/h severe	
Truong et al. [21], 2012.	US	retrospective	2006-2009	5.6 7	39/80 naive 41/80 post AT	AHI>1 abnormal	
Fung et al. [26], 2012.	Canada	retrospective case-control	2002-2012	7.1±4.4 7.6±4.1	23 naive Down 23 naive control	Pulse oximetry	
Ulualp et al. [15], 2013.	US	retrospective	2010-2012	6.0±3.7 (1.5-17)	82 naive	AHI 1-5 mild AHI 5-10	10 3 s 2

	moderate AHI>10 severe	di 1 di

n.r. not reported; naive: not operated; AT: adenoidectomy&tonsillectomy; DISE: Drug Induced Sleep Endosco
Obstructive Sleep Apnea; OAA: Obstructive Awake Apnea; VOTE classification [31].